DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration

Atlanta District Office
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November 10, 2004

VIA FEDERAL EXPRESS

Eric K. Mangiardi
President/ CEO
Alveolus, Inc.
401 N. Tryon Street
Charlotte, North Carolina 28202-2108

Warning Letter
(05-ATL-05)

Dear Mr. Mangiardi:

During an inspection of your firm located in Charlotte, North Carolina on July 13 through July 27, 2004, our investigator determined that your firm is a specifications developer and initial distributor for the Tracheal Bronchial Stent Technology System (TB-STS). This is a device as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that this system is adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for its manufacture, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements for medical devices which are set forth in the Quality System regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant violations include, but are not limited to, the following:

1. Failure to establish and maintain procedures for implementing corrective and preventive action including requirements for analyzing complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, as required by 21 CFR 820.100(a)(1). For example:

   a. Corrective and preventive action was not implemented following a complaint received revealing that polyurethane coating applied to a stent failed to cover all edges of the stent.
   b. Corrective and preventive action was not implemented following the receipt of four complaints involving the detachment of the stent sheath from the outer shaft during deployment.

2. Failure to verify or validate the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example, following the establishment of visual inspections for the polyurethane coating applied to the stents, two additional complaints were received.

3. Failure to have sufficient personnel with the necessary education, background, training, and experience to assure that all activities required by this part are correctly performed, as required

by 21 CFR 820.25(a). For example, there are currently no employees adequately trained to perform quality assessments and evaluations within the quality system.

4. Failure to establish and maintain procedures for acceptance of incoming product including inspecting, testing or otherwise verifying incoming product as conforming to specified requirements, as required by 21 CFR 820.80(b). For example, there are no acceptance procedures for incoming product to include verification of conformance to specifications for the Tracheal Bronchial Stent Technology Systems (TB-STS) devices.

5. Failure to establish and maintain procedures for finished device acceptance ensuring that each production run, lot, or batch of finished devices meets acceptance criteria, as required by 820.80(d). For example, there are no final release inspection procedures for the Tracheal Bronchial Stent Technology Systems (TB-STS) devices.

6. Failure to establish and maintain a Design History File (DHF) for each type of device containing or referencing the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements of this part, as required by 21 CFR 820.30(j). For example, the DHF does not contain:

   a. A product concept report defined in your written procedures.
   b. Detailed Phase I tasks and schedules, Test Market Study, and Design Review.
   c. The feasibility and development checklist approved by the Design Team prior to proceeding to the next stage.
   d. The design plan reviewed and approved by the Development Team and the President/CEO.

7. Failure to document results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation in the DHF as required by 21 CFR 820.30(g). For example:

   a. The detailed information on the study of a traumatic insertion in animal models as specified in the design requirements were not included in the DHF.
   b. The study design and acceptance criterion were not defined and available test information was incomplete in the DHF.
   c. There was not a protocol or study summary included in the DHF.

8. Failure to establish a quality plan which defines the quality practices, resources, and activities relevant to devices that are designed and manufactured, including how the requirements for quality will be met, as required by 21 CFR 820.20(d). There is no established quality plan defining the quality practices, resources, and activities relevant to devices that are designed and manufactured.

9. Failure to establish and maintain a valid statistical rationale for sampling plans to ensure that sampling methods are adequate for their intended use, that when changes occur the sampling plans are reviewed, and to document these activities, as required by 21 CFR 820.250(b). For example, [redacted] stent delivery systems were evaluated for mechanical properties, [redacted] samples were evaluated for guidewire compatibility, [redacted] samples were tested for stent deployment accuracy, and [redacted] samples were tested for flexibility with no statistical rationale supporting the sample sizes.

10. Failure to evaluate and select potential suppliers, contractors, and consultants on the basis of their ability to meet specified requirements, including quality requirements, as required by 21 CFR 820.50(a)(1). For example, no site visits have been performed at the contract manufacturers as specified in your written procedures for supplier selection.

The inspection also revealed that the Tracheal Bronchial Stent Technology System (TB-STS) is misbranded within the meaning of section 502(t)(2) of the Act in that your firm failed or refused to furnish material or information required by or under section 519 respecting the device and 21 CFR Part 803 (Medical Device Reporting regulation). Your firm failed to file adverse event reports as required by 21 CFR 803.50(a)(1) and (2). Specifically, your firm failed to promptly report to the FDA at least two MDR reportable malfunctions, one of which may have caused or contributed to a death or serious injury, involving stent ends which aligned themselves opposite one another and stuck together causing the stents to collapse. In one instance, the physician removed the stent from the patient, while in the other instance, the patient became cyanotic and explanted the device by coughing.

The inspection also revealed that the Tracheal Bronchial Stent Technology System (TB-STS) is misbranded within the meaning of section 502(t)(2) of the Act in that your firm failed or refused to furnish any material or information required by or under section 519 respecting the device and 21 CFR Part 806 (Reports of Corrections and Removals), that requires manufacturers and importers to promptly report to FDA, within 10 working days, any corrections or removals of a device to reduce a risk to health posed by the device. Our inspection revealed that your firm decided to remove the Tracheal-Bronchial Stent Technology System (TB-STS) from the market due to design and manufacturing defects and also following the receipt of reports of malfunctions and two deaths. You did not notify FDA in writing of your decision to cease the human use of this device.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your quality system.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for class III devices to which the Quality System regulation deficiencies are reasonably related will be cleared or approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

We acknowledge receipt of your letter dated August 25, 2004. Your response is under review and will be addressed in a separate letter. You may refer to your response in your answer to this Warning Letter. Please send your response to the attention of Serene N. Ackall, Compliance Officer, at the address noted in the letterhead. If you have any questions about this letter, you can contact Ms. Ackall at 404-253-1296.

Sincerely,

Mary Woleske

Mary Woleske
Director
Atlanta District Office